



UNITED STATES ENVIRONMENTAL PROTECTION AGENCY  
OFFICE OF RESEARCH AND DEVELOPMENT  
NATIONAL HEALTH AND ENVIRONMENTAL EFFECTS  
RESEARCH LABORATORY  
RESEARCH TRIANGLE PARK, NC 27711

Neurotoxicology Division, MD-74B

MEMORANDUM.

Date: 27 January 1999

Subject: Analysis of the Brain Morphometry Data from the Neurobehavioral Developmental Study of Ammonium Perchlorate (Argus, 1998a)

From: Andrew M. Geller Neurotoxicology Division, MD-74B  
National Health Effects and Environmental Research Laboratory

To: Annie Jarabek  
National Center for Environmental Assessment

Attached is the statistical analysis of the hormone data from the Argus Neurobehavioral Developmental Study (Argus Protocol #1613-002). Data was received from Argus on November 5, 1998 (York, 1998d) and imported in ASCII form to SAS for further analysis. I have attached a description of how the analyses were done, a description of results, and summary graphs.

## Analyses of Brain Morphometry Data from Neurobehavioral Developmental Study (Argus, 1998a)

**Summary:** A memo from Argus Laboratories (York, 1998d) contains brain morphometry data from the control, 3 mg/kg/day and 10 mg/kg/day dose groups from the Neurobehavioral Developmental Study of ammonium perchlorate in the rat at post-natal day 12 in the F1 generation (Argus, 1998a). This memo adds the morphometric data from the 3 mg/kg/day data to that of the control and high dose (10 mg/kg/day) groups previously reported in Tables 1 and 2 of Appendix P (Argus, 1998a). This data had been requested by the USEPA after initial findings of a morphometric increase in the size of the corpus callosum in the high dose group relative to controls. At the time that the report on Perchlorate Environmental Contamination had been prepared for External Review, only the data from the corpus callosum had been re-analyzed by the USEPA (Crofton, 1998c). The results of analysis of the morphometry data from the other brain regions is reported here.

Data was analyzed using a 2-way analysis of variance, with dose and sex as independent variables. It is desirable in the analysis of developmental data to have litter information; since none was included in Appendix P (Argus, 1998a) or the memo (York, 1998d), it is possible that the effects of sex and litter are confounded.

Significant effects of dose were found in corpus callosum, hippocampal gyrus, anterior/posterior cerebellum, and caudate putamen. An effect of sex was also found in caudate putamen.

The corpus callosum showed an increase in size at the highest dose tested (10 mg/kg /day). The other significant dose effects were driven by effects at the 3.0 mg/kg/day dose group. There was a significant decrease in size in this dose group in hippocampal gyrus and caudate putamen and a significant increase in size in anterior/posterior cerebellum.

**Data:** All data were supplied in the form of a memo (York, 1998d). Data were keyed in and entered as ASCII files for analyses by SAS.

Data for dependent measures (brain weight, anterior/posterior cerebrum, anterior/posterior cerebellum, frontal cortex, parietal cortex, caudate putamen, corpus callosum, hippocampal gyrus, cerebellum, external germinal layer) were subjected to separate two-way ANOVAs. Treatment (dose) and sex were the independent between-subjects variables. Mean contrasts were performed using Tukey's Studentized Range (HSD) Test. Where there was a dose x sex interaction, separate one-way ANOVAs were run for each gender.

To correct for multiple comparisons the acceptable alpha for significance (for all interaction main effects tests) was corrected to 0.016 (alpha of 0.05 divided by the square root of the number of ANOVAs).

## Analyses of Brain Morphometry Data from Neurobehavioral Developmental Study (Argus, 1998a)

**Summary:** A memo from Argus Laboratories (York, 1998d) contains brain morphometry data from the control, 3 mg/kg/day and 10 mg/kg/day dose groups from the Neurobehavioral Developmental Study of ammonium perchlorate in the rat at post-natal day 12 in the F1 generation (Argus, 1998a). This memo adds the morphometric data from the 3 mg/kg/day data to that of the control and high dose (10 mg/kg/day) groups previously reported in Tables 1 and 2 of Appendix P (Argus, 1998a). This data had been requested by the USEPA after initial findings of a morphometric increase in the size of the corpus callosum in the high dose group relative to controls. At the time that the report on Perchlorate Environmental Contamination had been prepared for External Review, only the data from the corpus callosum had been re-analyzed by the USEPA (Crofton, 1998c). The results of analysis of the morphometry data from the other brain regions is reported here.

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*Data Analysis - Results:*

Significant effects of dose were found in corpus callosum, hippocampal gyrus, anterior/posterior cerebellum, and caudate putamen (Figure 1). An effect of sex was also found in caudate putamen.

Corpus callosum showed an increase in size in the 10 mg/kg/day dose group, as previously reported in Crofton (1998c).

Hippocampal gyrus (12% less than control) and caudate putamen (7.3% less than control) showed a decrease in size at the 3 mg/kg/day dose, with no significant difference between control and high dose, yielding a U-shaped dose response. A/P cerebellum showed a significant increase in size in the 3 mg/kg/day group (13% greater than control), yielding an inverted U-shaped dose response function.

Inhibition of iodide uptake is highly non-linear and saturable, and therefore does not rule out the possibility of a U-shaped dose response. Until the PBPK modeling better characterizes this phenomenon, we are not requesting histopathological evaluation of brain sections at the next lower dose. This is pending commentary with respect to the potential for U-shaped dose response for changes in brain morphology with perchlorate exposure and other recommendations made at the external peer review. We do request, however, that the tissue samples be saved until a final decision is made on this matter.

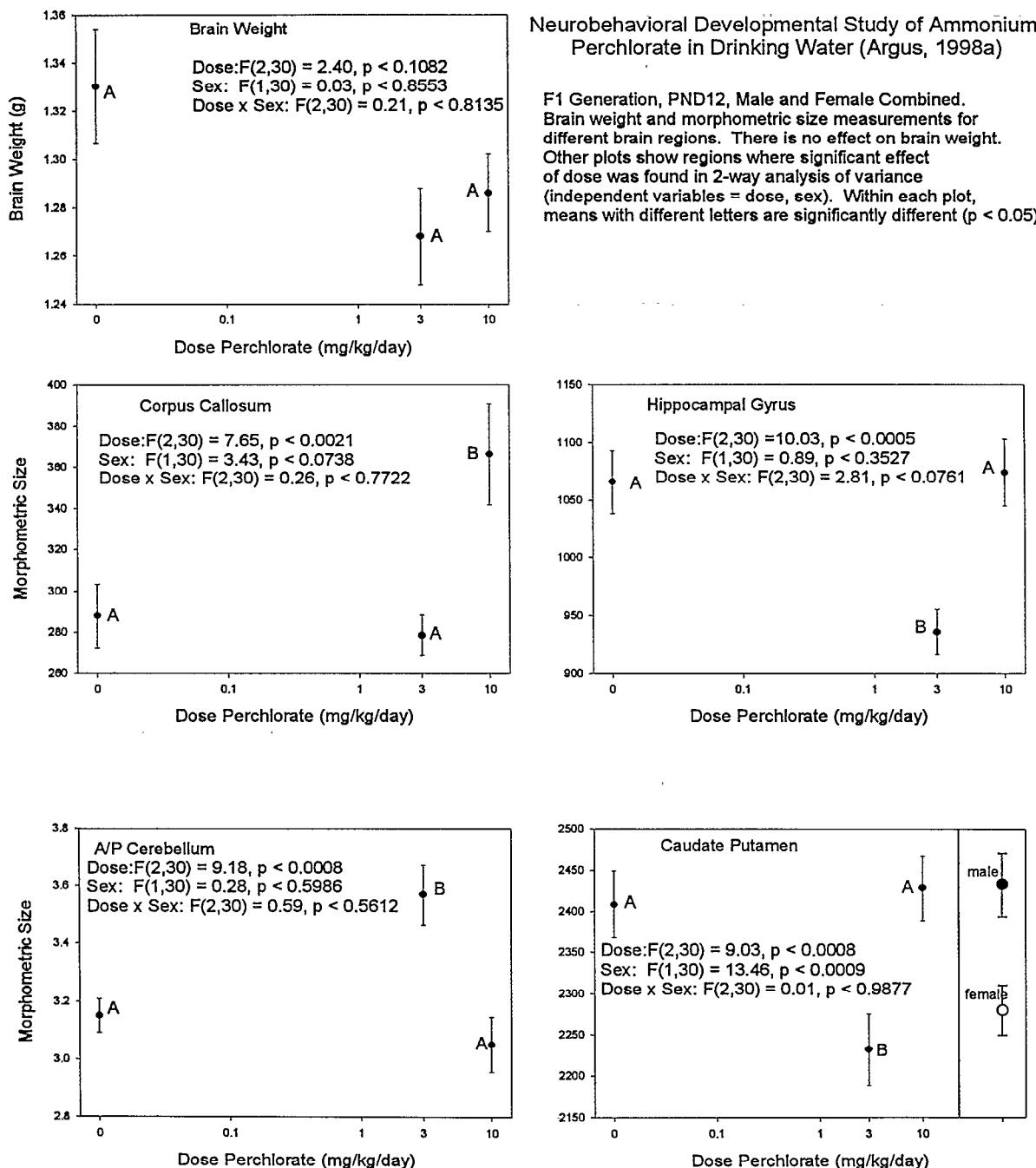


Figure 1

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The SAS System

15:56 Tuesday, January 26, 1999

NOTE: Copyright (c) 1989-1996 by SAS Institute Inc., Cary, NC, USA.  
NOTE: SAS (r) Proprietary Software Release 6.12 TS020  
Licensed to US ENVIRONMENTAL PROTECTION AGENCY, Site 0019614059.

NOTE: Running on ALPHASERVER Model 2100 5/300 Serial Number 80000000.

WARNING: Your system is scheduled to expire on February 18, 1999, which is 23 days from now. Please contact your installation representative to have your system renewed. The SAS system will no longer function on or after that date.  
Welcome to the NHEERL-RTP SAS Information Delivery System.

```
1      *THIS FILE IS FOUND AT [CROfton.THYROID.perchlorate]perchlorate_dn_pnd5.SAS;
2      *IT ANALYZES THE THYROID HORMONE DATA FROM THE WPAFB 90 DAY PERCHLORATE STUDY;
3
4
5      *INPUT DATA INTO SAS DATASET;
6      DATA RAW; INFILE '[GELLER.BMD]1613-002.Txt';
7      INPUT SEX$ DOSE$ RATNO BRAINWT CEREBRUM APCBLM FCORTEX PCORTEX
8          CAUDPUT CORPCOL HIPPO CEREBLL XGEM;
9
10     * BRAINWT = TOTAL BRAIN WEIGHT;
11     * CEREBRUM = ANTER/POST CEREBRUM;
12     * APCBLM = ANT/POST CEREBELLUM;
13     * FCORTEX = FRONTAL CORTEX;
14     * PCORTEX = PARIETAL CORTEX;
15     * CAUDPUT = CAUDATE PUTAMEN;
16     * CORPCOL = CORPUS CALLOSUM;
17     * HIPPO = HIPPOCAMPAL GYRUS;
18     * CEREBLL = CEREBELLUM;
19     * XGEM = EXT GERM LAYER;
20
21     *ASSIGN TREATMENT VALUES TO DOSE CODES;
22     IF DOSE = '1' THEN TRT = '1-----CONTROL';
23     IF DOSE = '2' THEN TRT = '2--0.1_mg/kg/day';
24     IF DOSE = '3' THEN TRT = '3--1.0_mg/kg/day';
25     IF DOSE = '4' THEN TRT = '4--3.0_mg/kg/day';
26     IF DOSE = '5' THEN TRT = '5-10.0_mg/kg/day';
27
```

NOTE: The infile '[GELLER.BMD]1613-002.Txt' is:  
File=DSA21:[SASS\$USERS.GELLER.BMD]1613-002.TXT

NOTE: 36 records were read from the infile '[GELLER.BMD]1613-002.Txt'.  
The minimum record length was 73.  
The maximum record length was 73.

NOTE: The data set WORK.RAW has 36 observations and 14 variables.

```
28      PROC PRINT;
```



50 PROC SORT; BY TRT SEX;  
WARNING: The BASE Product product with which SORT is associated will expire within 30 days. Please contact your SAS installation  
representative to have it renewed.

51

NOTE: Input data set is already sorted, no sorting done.

51 PROC GLM;

WARNING: The SAS/STAT product with which GLM is associated will expire within 30 days. Please contact your SAS installation  
representative to have it renewed.

52 CLASSES TRT SEX;

53 MODEL BRAINWT CEREBRUM APCBLM FCORTEX PCORTEX CAUDPUT

54 CORPCOL HIPPO CEREBLL XGEM = TRT|SEX;

55 MEANS TRT/TUKEY LINES;

13 The SAS System 15:56 Tuesday, January 26, 1999

56 TITLE1 "ARGUS DEVELOPMENTAL NEURO PND12 CNS MORPHOMETRICS";

57 TITLE2 "PROC GLM - WITH TUKEYS";

58 ENDSAS;

NOTE: Means from the MEANS statement are not adjusted for other terms in the model. For adjusted means, use the LSMEANS statement.  
NOTE: The PROCEDURE GLM printed pages 5-25.

NOTE: SAS Institute Inc., SAS Campus Drive, Cary, NC USA 27513-2414

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OBS	SEX	DOSE	RATNO	BRAINWT	CEREBRUM	APCBLM	FCORTEX	PCORTEX	CAUDPUT	CORPCOL	HIPPO	CEREBLL	XGEM	TRT
1	F	1	2122	1.233	12.6	3.0	1224	1344	2208	192	912	3120	43	1-----CONTROL
2	F	1	2136	1.365	12.8	3.5	1512	1440	2448	259	1056	3696	36	1-----CONTROL
3	F	1	2170	1.342	12.9	3.0	1584	1512	2304	288	1104	3600	41	1-----CONTROL
4	F	1	2172	1.517	13.5	3.0	1632	1536	2496	298	1128	3984	41	1-----CONTROL
5	F	1	2185	1.321	12.5	3.2	1416	1296	2208	269	1152	3552	48	1-----CONTROL
6	F	1	2194	1.280	12.5	2.9	1536	1488	2304	336	960	3552	41	1-----CONTROL
7	F	2	2132	1.259	12.6	4.0	1440	1392	2304	259	984	3360	48	2--0.1_mg/kg/day
8	F	2	2133	1.168	12.3	3.7	1440	1392	2160	269	840	3072	46	2--0.1_mg/kg/day
9	F	2	2145	1.419	13.2	3.3	1560	1656	2256	288	1008	3840	41	2--0.1_mg/kg/day
10	F	2	2151	1.212	12.8	3.5	1488	1416	2016	269	1080	3456	41	2--0.1_mg/kg/day
11	F	2	2165	1.222	12.5	3.3	1488	1488	2064	259	912	3360	41	2--0.1_mg/kg/day
12	F	2	2174	1.347	13.2	4.1	1440	1392	2160	250	960	3696	43	2--0.1_mg/kg/day
13	F	3	2123	1.278	12.4	3.4	1344	1392	2304	307	1080	3024	41	3--1.0_mg/kg/day
14	F	3	2124	1.310	12.9	3.0	1296	1440	2400	336	1032	3552	36	3--1.0_mg/kg/day
15	F	3	2140	1.182	12.6	3.0	1464	1464	2352	355	1056	3264	36	3--1.0_mg/kg/day
16	F	3	2143	1.254	12.9	3.0	2198	1440	2448	346	1008	3168	36	3--1.0_mg/kg/day
17	F	3	2193	1.314	12.6	2.9	1392	1512	2256	355	936	3696	41	3--1.0_mg/kg/day
18	F	3	2198	1.330	13.2	3.3	1632	1608	2352	326	1008	3504	41	3--1.0_mg/kg/day
19	M	1	2002	1.375	13.2	3.4	1440	1416	2592	278	1080	3888	41	1-----CONTROL
20	M	1	2008	1.213	12.7	3.2	1296	1344	2400	240	1056	3648	36	1-----CONTROL
21	M	1	2036	1.357	12.7	3.2	1224	1368	2640	336	1248	3552	36	1-----CONTROL
22	M	1	2062	1.252	12.5	2.9	1368	1368	2352	240	936	3168	41	1-----CONTROL
23	M	1	2067	1.389	13.0	3.4	1368	1392	2544	384	1080	3696	41	1-----CONTROL
24	M	1	2094	1.335	13.2	3.1	1560	1632	2400	336	1080	3216	36	1-----CONTROL
25	M	2	2001	1.335	13.0	3.5	1464	1440	2400	365	984	3456	41	2--0.1_mg/kg/day
26	M	2	2019	1.289	13.0	3.5	1440	1440	2496	307	912	3312	36	2--0.1_mg/kg/day
27	M	2	2026	1.240	13.1	3.1	1392	1368	2304	259	888	3360	34	2--0.1_mg/kg/day
28	M	2	2039	1.250	13.1	3.8	1512	1488	2304	307	912	3312	31	2--0.1_mg/kg/day
29	M	2	2076	1.267	12.6	4.0	1272	1464	2016	240	864	3216	24	2--0.1_mg/kg/day
30	M	2	2097	1.208	12.3	3.0	1464	1464	2304	269	888	3264	43	2--0.1_mg/kg/day
31	M	3	2010	1.356	13.0	3.2	1608	1584	2640	528	1152	3504	36	3--1.0_mg/kg/day
32	M	3	2020	1.194	13.0	3.0	1584	1464	2688	317	984	3168	41	3--1.0_mg/kg/day
33	M	3	2028	1.249	12.7	2.2	1080	1296	2544	557	1200	3120	36	3--1.0_mg/kg/day
34	M	3	2037	1.353	13.0	3.5	1344	1512	2400	307	1032	3792	36	3--1.0_mg/kg/day
35	M	3	2041	1.289	13.0	3.2	1080	1440	2304	298	1104	3216	41	3--1.0_mg/kg/day
36	M	3	2043	1.321	13.0	2.9	1080	1488	2448	365	1296	3744	41	3--1.0_mg/kg/day

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 GROUP MEANS BY TREATMENT

----- TRT=1 ----- CONTROL -----

Variable	N	Mean	Std Error	Minimum	Maximum	Std Dev	Variance	CV
BRAINWT	12	1.3315833	0.0237300	1.2130000	1.5170000	0.0822031	0.0067574	6.1733379
CEREBRUM	12	12.8416667	0.0941134	12.5000000	13.5000000	0.3260182	0.1062879	2.5387532
APCBLM	12	3.1500000	0.0583874	2.9000000	3.5000000	0.2022600	0.0409091	6.4209511
FCORTEX	12	1430.00	39.9044313	1224.00	1632.00	138.2330049	19108.36	9.6666437
PCORTEX	12	1428.00	28.1037041	1296.00	1632.00	97.3540866	9477.82	6.8175131
CAUDPUT	12	2408.00	40.8634088	2208.00	2640.00	141.5550006	20037.82	5.8785299
CORPCOL	12	288.0000000	15.4120181	192.0000000	384.0000000	53.3087969	2850.36	18.5377767
HIPPO	12	1066.00	27.3096719	912.0000000	1248.00	94.6034787	8949.82	8.8746228
CEREBLL	12	3556.00	77.8156329	3120.00	3984.00	269.5612597	72663.27	7.5804629
XGEM	12	40.0833333	1.0405297	36.0000000	48.0000000	3.6045006	12.9924242	8.9925170

----- TRT=2--0.1\_mg/kg/day -----

Variable	N	Mean	Std Error	Minimum	Maximum	Std Dev	Variance	CV
BRAINWT	12	1.2680000	0.0202286	1.1680000	1.4190000	0.0700740	0.0049104	5.5263397
CEREBRUM	12	12.8083333	0.0972799	12.3000000	13.2000000	0.3369875	0.1135606	2.6310023
APCBLM	12	3.5666667	0.1039619	3.0000000	4.1000000	0.3601347	0.1296970	10.0972333
FCORTEX	12	1450.00	20.3514574	1272.00	1560.00	70.4995164	4970.18	4.8620356
PCORTEX	12	1450.00	22.0000000	1368.00	1656.00	76.2102355	5808.00	5.2558783
CAUDPUT	12	2232.00	43.6181780	2016.00	2496.00	151.0978010	22830.55	6.7696147
CORPCOL	12	278.4166667	9.8868280	240.0000000	365.0000000	34.2489770	1172.99	12.3013386
HIPPO	12	936.0000000	19.8173478	840.0000000	1080.00	68.6493064	4712.73	7.3343276
CEREBLL	12	3392.00	59.4765041	3072.00	3840.00	206.0326541	42449.45	6.0740759
XGEM	12	39.0833333	1.9480306	24.0000000	48.0000000	6.7481760	45.5378788	17.2661219

----- TRT=3--1.0\_mg/kg/day -----

Variable	N	Mean	Std Error	Minimum	Maximum	Std Dev	Variance	CV
BRAINWT	12	1.2858333	0.0164353	1.1820000	1.3560000	0.0569335	0.0032414	4.4277517
CEREBRUM	12	12.8583333	0.0668086	12.4000000	13.2000000	0.2314316	0.0535606	1.7998572
APCBLM	12	3.0500000	0.0957427	2.2000000	3.5000000	0.3316625	0.1100000	10.8741796
FCORTEX	12	1425.17	90.8126471	1080.00	2198.00	314.5842374	98963.24	22.0735051
PCORTEX	12	1470.00	23.8403783	1296.00	1608.00	82.5854929	6820.36	5.6180607
CAUDPUT	12	2428.00	38.9498512	2256.00	2688.00	134.9262425	18205.09	5.5570940
CORPCOL	12	366.4166667	24.5956569	298.0000000	557.0000000	85.2018548	7259.36	23.2527236
HIPPO	12	1074.00	29.1141952	936.0000000	1296.00	100.8545307	10171.64	9.3905522
CEREBLL	12	3396.00	77.0643179	3024.00	3792.00	266.9586281	71266.91	7.8609726
XGEM	12	38.5000000	0.7537784	36.0000000	41.0000000	2.6111648	6.8181818	6.7822463

1

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 GROUP MEANS BY GENDER AND TREATMENT

----- TRT=1 ----- CONTROL SEX=F -----

Variable	N	Mean	Std Error	Minimum	Maximum	Std Dev	Variance	CV
BRAINWT	6	1.3430000	0.0397131	1.2330000	1.5170000	0.0972769	0.0094628	7.2432557
CEREBRUM	6	12.8000000	0.1549193	12.5000000	13.5000000	0.3794733	0.1440000	2.9646353
APCBLM	6	3.1000000	0.0894427	2.9000000	3.5000000	0.2190890	0.0480000	7.0673878
FCORTEX	6	1484.00	59.8932383	1224.00	1632.00	146.7078730	21523.20	9.8859753
PCORTEX	6	1436.00	39.3954312	1296.00	1536.00	96.4987047	9312.00	6.7199655
CAUDPUT	6	2328.00	49.1853637	2208.00	2496.00	120.4790438	14515.20	5.1752167
CORPCOL	6	273.6666667	19.6547987	192.0000000	336.0000000	48.1442278	2317.87	17.5922879
HIPPO	6	1052.00	39.3954312	912.0000000	1152.00	96.4987047	9312.00	9.1728807
CEREBLL	6	3584.00	114.0385900	3120.00	3984.00	279.3363564	78028.80	7.7939832
XGEM	6	41.6666667	1.5846486	36.0000000	48.0000000	3.8815804	15.0666667	9.3157930

----- TRT=1 ----- CONTROL SEX=M -----

Variable	N	Mean	Std Error	Minimum	Maximum	Std Dev	Variance	CV
BRAINWT	6	1.3201667	0.0291278	1.2130000	1.3890000	0.0713482	0.0050906	5.4044848
CEREBRUM	6	12.8833333	0.1194897	12.5000000	13.2000000	0.2926887	0.0856667	2.2718397
APCBLM	6	3.2000000	0.0774597	2.9000000	3.4000000	0.1897367	0.0360000	5.9292706
FCORTEX	6	1376.00	47.4636703	1224.00	1560.00	116.2617736	13516.80	8.4492568
PCORTEX	6	1420.00	43.5614508	1344.00	1632.00	106.7033270	11385.60	7.5143188
CAUDPUT	6	2488.00	48.6621002	2352.00	2640.00	119.1973154	14208.00	4.7908889
CORPCOL	6	302.3333333	24.0134222	240.0000000	384.0000000	58.8206313	3459.87	19.4555561
HIPPO	6	1080.00	40.6349603	936.0000000	1248.00	99.5349185	9907.20	9.2161962
CEREBLL	6	3528.00	115.4330975	3168.00	3888.00	282.7521883	79948.80	8.0145178
XGEM	6	38.5000000	1.1180340	36.0000000	41.0000000	2.7386128	7.5000000	7.1132800

----- TRT=2--0.1\_mg/kg/day SEX=F -----

Variable	N	Mean	Std Error	Minimum	Maximum	Std Dev	Variance	CV
BRAINWT	6	1.2711667	0.0384339	1.1680000	1.4190000	0.0941433	0.0088630	7.4060572
CEREBRUM	6	12.7666667	0.1520234	12.3000000	13.2000000	0.3723797	0.1386667	2.9168125
APCBLM	6	3.6500000	0.1408309	3.3000000	4.1000000	0.3449638	0.1190000	9.4510621
FCORTEX	6	1476.00	19.3494186	1440.00	1560.00	47.3962024	2246.40	3.2111248
PCORTEX	6	1456.00	42.7831743	1392.00	1656.00	104.7969465	10982.40	7.1975925
CAUDPUT	6	2160.00	44.6855681	2016.00	2304.00	109.4568408	11980.80	5.0674463
CORPCOL	6	265.6666667	5.3395797	250.0000000	288.0000000	13.0792456	171.0666667	4.9231790
HIPPO	6	964.0000000	33.6095225	840.0000000	1080.00	82.3261805	6777.60	8.5400602
CEREBLL	6	3464.00	111.1395519	3072.00	3840.00	272.2351924	74112.00	7.8589836
XGEM	6	43.3333333	1.2292726	41.0000000	48.0000000	3.0110906	9.0666667	6.9486706

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GROUP MEANS BY GENDER AND TREATMENT

----- TRT=2--0.1\_mg/kg/day SEX=M -----

Variable	N	Mean	Std Error	Minimum	Maximum	Std Dev	Variance	CV
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BRAINWT	6	1.2648333	0.0178688	1.2080000	1.3350000	0.0437695	0.0019158	3.4604932
CEREBRUM	6	12.8500000	0.1335415	12.3000000	13.1000000	0.3271085	0.1070000	2.5455918
APCBLM	6	3.4833333	0.1579381	3.0000000	4.0000000	0.3868678	0.1496667	11.1062516
FCORTEX	6	1424.00	34.3161769	1272.00	1512.00	84.0571234	7065.60	5.9028879
PCORTEX	6	1444.00	16.8760185	1368.00	1488.00	41.3376342	1708.80	2.8627170
CAUDPUT	6	2304.00	65.5804849	2016.00	2496.00	160.6387251	25804.80	6.9721669
CORPCOL	6	291.1666667	18.3456020	240.0000000	365.0000000	44.9373638	2019.37	15.4335537
HIPPO	6	908.0000000	16.8760185	864.0000000	984.0000000	41.3376342	1708.80	4.5526029
CEREBLL	6	3320.00	33.7520370	3216.00	3456.00	82.6752684	6835.20	2.4902189
XGEM	6	34.8333333	2.8215441	24.0000000	43.0000000	6.9113433	47.7666667	19.8411770

----- TRT=3--1.0\_mg/kg/day SEX=F -----

Variable	N	Mean	Std Error	Minimum	Maximum	Std Dev	Variance	CV
BRAINWT	6	1.2780000	0.0222231	1.1820000	1.3300000	0.0544353	0.0029632	4.2594118
CEREBRUM	6	12.7666667	0.1173788	12.4000000	13.2000000	0.2875181	0.0826667	2.2521001
APCBLM	6	3.1000000	0.0816497	2.9000000	3.4000000	0.2000000	0.0400000	6.4516129
FCORTEX	6	1554.33	137.3350324	1296.00	2198.00	336.4007531	113165.47	21.6427677
PCORTEX	6	1476.00	30.8285582	1392.00	1608.00	75.5142371	5702.40	5.1161407
CAUDPUT	6	2352.00	27.7128129	2256.00	2448.00	67.8822510	4608.00	2.8861501
CORPCOL	6	337.5000000	7.6365350	307.0000000	355.0000000	18.7056141	349.9000000	5.5424042
HIPPO	6	1020.00	20.3174802	936.0000000	1080.00	49.7674592	2476.80	4.8791627
CEREBLL	6	3368.00	104.7358582	3024.00	3696.00	256.5494104	65817.60	7.6172628
XGEM	6	38.5000000	1.1180340	36.0000000	41.0000000	2.7386128	7.5000000	7.1132800

----- TRT=3--1.0\_mg/kg/day SEX=M -----

Variable	N	Mean	Std Error	Minimum	Maximum	Std Dev	Variance	CV
BRAINWT	6	1.2936667	0.0258865	1.1940000	1.3560000	0.0634087	0.0040207	4.9014734
CEREBRUM	6	12.9500000	0.0500000	12.7000000	13.0000000	0.1224745	0.0150000	0.9457489
APCBLM	6	3.0000000	0.1807392	2.2000000	3.5000000	0.4427189	0.1960000	14.7572957
FCORTEX	6	1296.00	103.6918512	1080.00	1608.00	253.9921259	64512.00	19.5981579
PCORTEX	6	1464.00	39.1918359	1296.00	1584.00	96.0000000	9216.00	6.5573770
CAUDPUT	6	2504.00	59.9733274	2304.00	2688.00	146.9040503	21580.80	5.8667752
CORPCOL	6	395.3333333	47.6337882	298.0000000	557.0000000	116.6784756	13613.87	29.5139483
HIPPO	6	1128.00	46.3724056	984.0000000	1296.00	113.5887318	12902.40	10.0699230
CEREBLL	6	3424.00	121.8523697	3120.00	3792.00	298.4761297	89088.00	8.7171767
XGEM	6	38.5000000	1.1180340	36.0000000	41.0000000	2.7386128	7.5000000	7.1132800

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PROC GLM - WITH TUKEYS

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General Linear Models Procedure  
Class Level Information

Class	Levels	Values
TRT	3	1-----CONTROL 2--0.1_mg/kg/day 3--1.0_mg/kg/day
SEX	2	F M

Number of observations in data set = 36

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ARGUS DEVELOPMENTAL NEURO PND12 CNS MORPHOMETRICS  
PROC GLM - WITH TUKEYS

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## General Linear Models Procedure

Dependent Variable: BRAINWT

Source	DF	Sum of Squares	Mean Square	F Value	Pr > F
Model	5	0.02823647	0.00564729	1.05	0.4079
Error	30	0.16157983	0.00538599		
Corrected Total	35	0.18981631			
		R-Square	C.V.	Root MSE	BRAINWT Mean
		0.148757	5.666522	0.07338933	1.29513889
Source	DF	Type I SS	Mean Square	F Value	Pr > F
TRT	2	0.02581572	0.01290786	2.40	0.1082
SEX	1	0.00018225	0.00018225	0.03	0.8553
TRT*SEX	2	0.00223850	0.00111925	0.21	0.8135
Source	DF	Type III SS	Mean Square	F Value	Pr > F
TRT	2	0.02581572	0.01290786	2.40	0.1082
SEX	1	0.00018225	0.00018225	0.03	0.8553
TRT*SEX	2	0.00223850	0.00111925	0.21	0.8135

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ARGUS DEVELOPMENTAL NEURO PND12 CNS MORPHOMETRICS  
PROC GLM - WITH TUKEYS

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## General Linear Models Procedure

Dependent Variable: CEREBRUM

Source	DF	Sum of Squares	Mean Square	F Value	Pr > F
Model	5	0.15805556	0.03161111	0.33	0.8902
Error	30	2.86500000	0.09550000		
Corrected Total	35	3.02305556			
		R-Square	C.V.	Root MSE	CEREBRUM Mean
		0.052283	2.407511	0.30903074	12.83611111
Source	DF	Type I SS	Mean Square	F Value	Pr > F
TRT	2	0.01555556	0.00777778	0.08	0.9220
SEX	1	0.12250000	0.12250000	1.28	0.2664
TRT*SEX	2	0.02000000	0.01000000	0.10	0.9009
Source	DF	Type III SS	Mean Square	F Value	Pr > F
TRT	2	0.01555556	0.00777778	0.08	0.9220
SEX	1	0.12250000	0.12250000	1.28	0.2664
TRT*SEX	2	0.02000000	0.01000000	0.10	0.9009

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ARGUS DEVELOPMENTAL NEURO PND12 CNS MORPHOMETRICS  
PROC GLM - WITH TUKEYS

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## General Linear Models Procedure

Dependent Variable: APCBLM

Source	DF	Sum of Squares	Mean Square	F Value	Pr > F
Model	5	1.94555556	0.38911111	3.97	0.0070
Error	30	2.94333333	0.09811111		
Corrected Total	35	4.88888889			
	R-Square	C.V.	Root MSE		APCBLM Mean
	0.397955	9.621305	0.31322693		3.25555556
Source	DF	Type I SS	Mean Square	F Value	Pr > F
TRT	2	1.80222222	0.90111111	9.18	0.0008
SEX	1	0.02777778	0.02777778	0.28	0.5986
TRT*SEX	2	0.11555556	0.05777778	0.59	0.5612
Source	DF	Type III SS	Mean Square	F Value	Pr > F
TRT	2	1.80222222	0.90111111	9.18	0.0008
SEX	1	0.02777778	0.02777778	0.28	0.5986
TRT*SEX	2	0.11555556	0.05777778	0.59	0.5612

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ARGUS DEVELOPMENTAL NEURO PND12 CNS MORPHOMETRICS  
PROC GLM - WITH TUKEYS

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## General Linear Models Procedure

Dependent Variable: FCORTEX

Source	DF	Sum of Squares	Mean Square	F Value	Pr > F
Model	5	247472.55555554	49494.51111111	1.34	0.2756
Error	30	1110147.33333334	37004.91111111		
Corrected Total	35	1357619.88888888			
		R-Square	C.V.	Root MSE	FCORTEX Mean
		0.182284	13.40482	192.36660602	1435.05555556
Source	DF	Type I SS	Mean Square	F Value	Pr > F
TRT	2	4160.22222222	2080.11111111	0.06	0.9454
SEX	1	175002.77777778	175002.77777778	4.73	0.0377
TRT*SEX	2	68309.55555556	34154.77777778	0.92	0.4083
Source	DF	Type III SS	Mean Square	F Value	Pr > F
TRT	2	4160.22222222	2080.11111111	0.06	0.9454
SEX	1	175002.77777778	175002.77777778	4.73	0.0377
TRT*SEX	2	68309.55555556	34154.77777778	0.92	0.4083

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ARGUS DEVELOPMENTAL NEURO PND12 CNS MORPHOMETRICS  
PROC GLM - WITH TUKEYS

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## General Linear Models Procedure

Dependent Variable: PCORTEX

Source	DF	Sum of Squares	Mean Square	F Value	Pr > F
Model	5	12224.0000000	2444.80000000	0.30	0.9068
Error	30	241536.0000000	8051.20000000		
Corrected Total	35	253760.0000000			
		R-Square	C.V.	Root MSE	PCORTEX Mean
		0.048172	6.191017	89.72847931	1449.33333333
Source	DF	Type I SS	Mean Square	F Value	Pr > F
TRT	2	10592.0000000	5296.00000000	0.66	0.5253
SEX	1	1600.0000000	1600.00000000	0.20	0.6590
TRT*SEX	2	32.00000000	16.00000000	0.00	0.9980
Source	DF	Type III SS	Mean Square	F Value	Pr > F
TRT	2	10592.0000000	5296.00000000	0.66	0.5253
SEX	1	1600.0000000	1600.00000000	0.20	0.6590
TRT*SEX	2	32.00000000	16.00000000	0.00	0.9980

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ARGUS DEVELOPMENTAL NEURO PND12 CNS MORPHOMETRICS  
PROC GLM - WITH TUKEYS

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## General Linear Models Procedure

Dependent Variable: CAUDPUT

Source	DF	Sum of Squares	Mean Square	F Value	Pr > F
Model	5	487488.00000000	97497.60000000	6.31	0.0004
Error	30	463488.00000000	15449.60000000		
Corrected Total	35	950976.00000000			
R-Square		C.V.	Root MSE		CAUDPUT Mean
		0.512619	5.275739	124.29641990	2356.00000000
Source	DF	Type I SS	Mean Square	F Value	Pr > F
TRT	2	279168.00000000	139584.00000000	9.03	0.0008
SEX	1	207936.00000000	207936.00000000	13.46	0.0009
TRT*SEX	2	384.00000000	192.00000000	0.01	0.9877
Source	DF	Type III SS	Mean Square	F Value	Pr > F
TRT	2	279168.00000000	139584.00000000	9.03	0.0008
SEX	1	207936.00000000	207936.00000000	13.46	0.0009
TRT*SEX	2	384.00000000	192.00000000	0.01	0.9877

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ARGUS DEVELOPMENTAL NEURO PND12 CNS MORPHOMETRICS  
PROC GLM - WITH TUKEYS

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## General Linear Models Procedure

Dependent Variable: CORPCOL

Source	DF	Sum of Squares	Mean Square	F Value	Pr > F
Model	5	70390.2222222	14078.04444444	3.85	0.0082
Error	30	109659.6666667	3655.3222222		
Corrected Total	35	180049.8888889			
		R-Square	C.V.	Root MSE	CORPCOL Mean
		0.390948	19.44375	60.45926085	310.94444444
Source	DF	Type I SS	Mean Square	F Value	Pr > F
TRT	2	55940.05555556	27970.02777778	7.65	0.0021
SEX	1	12544.00000000	12544.00000000	3.43	0.0738
TRT*SEX	2	1906.16666667	953.08333333	0.26	0.7722
Source	DF	Type III SS	Mean Square	F Value	Pr > F
TRT	2	55940.05555556	27970.02777778	7.65	0.0021
SEX	1	12544.00000000	12544.00000000	3.43	0.0738
TRT*SEX	2	1906.16666667	953.08333333	0.26	0.7722

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ARGUS DEVELOPMENTAL NEURO PND12 CNS MORPHOMETRICS  
PROC GLM - WITH TUKEYS

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## General Linear Models Procedure

Dependent Variable: HIPPO

Source	DF	Sum of Squares	Mean Square	F Value	Pr > F
Model	5	190784.00000000	38156.80000000	5.31	0.0013
Error	30	215424.00000000	7180.80000000		
Corrected Total	35	406208.00000000			
					HIPPO Mean
		R-Square	C.V.	Root MSE	
		0.469671	8.264590	84.73960113	1025.33333333
Source	DF	Type I SS	Mean Square	F Value	Pr > F
TRT	2	144032.00000000	72016.00000000	10.03	0.0005
SEX	1	6400.00000000	6400.00000000	0.89	0.3527
TRT*SEX	2	40352.00000000	20176.00000000	2.81	0.0761
Source	DF	Type III SS	Mean Square	F Value	Pr > F
TRT	2	144032.00000000	72016.00000000	10.03	0.0005
SEX	1	6400.00000000	6400.00000000	0.89	0.3527
TRT*SEX	2	40352.00000000	20176.00000000	2.81	0.0761

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ARGUS DEVELOPMENTAL NEURO PND12 CNS MORPHOMETRICS  
PROC GLM - WITH TUKEYS

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## General Linear Models Procedure

Dependent Variable: CEREBLL

Source	DF	Sum of Squares	Mean Square	F Value	Pr > F
Model	5	291072.00000000	58214.40000000	0.89	0.5021
Error	30	1969152.00000000	65638.40000000		
Corrected Total	35	2260224.00000000			
		R-Square	C.V.	Root MSE	CEREBLL Mean
		0.128780	7.430392	256.19992194	3448.00000000

Source	DF	Type I SS	Mean Square	F Value	Pr > F
TRT	2	210048.00000000	105024.00000000	1.60	0.2186
SEX	1	20736.00000000	20736.00000000	0.32	0.5783
TRT*SEX	2	60288.00000000	30144.00000000	0.46	0.6361
Source	DF	Type III SS	Mean Square	F Value	Pr > F
TRT	2	210048.00000000	105024.00000000	1.60	0.2186
SEX	1	20736.00000000	20736.00000000	0.32	0.5783
TRT*SEX	2	60288.00000000	30144.00000000	0.46	0.6361

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ARGUS DEVELOPMENTAL NEURO PND12 CNS MORPHOMETRICS  
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## General Linear Models Procedure

Dependent Variable: XGEM

Source	DF	Sum of Squares	Mean Square	F Value	Pr > F
Model	5	262.22222222	52.44444444	3.33	0.0164
Error	30	472.00000000	15.73333333		
Corrected Total	35	734.22222222			
					XGEM Mean
R-Square		C.V.	Root MSE		
0.357143		10.11296	3.96652661		39.22222222
Source	DF	Type I SS	Mean Square	F Value	Pr > F
TRT	2	15.38888889	7.69444444	0.49	0.6180
SEX	1	136.11111111	136.11111111	8.65	0.0062
TRT*SEX	2	110.72222222	55.36111111	3.52	0.0424
Source	DF	Type III SS	Mean Square	F Value	Pr > F
TRT	2	15.38888889	7.69444444	0.49	0.6180
SEX	1	136.11111111	136.11111111	8.65	0.0062
TRT*SEX	2	110.72222222	55.36111111	3.52	0.0424

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ARGUS DEVELOPMENTAL NEURO PND12 CNS MORPHOMETRICS  
PROC GLM - WITH TUKEYS

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## General Linear Models Procedure

Tukey's Studentized Range (HSD) Test for variable: BRAINWT

NOTE: This test controls the type I experimentwise error rate, but generally has a higher type II error rate than REGWQ.

Alpha= 0.05 df= 30 MSE= 0.005386  
Critical Value of Studentized Range= 3.487  
Minimum Significant Difference= 0.0739

Means with the same letter are not significantly different.

Tukey Grouping	Mean	N	TRT
A	1.33158	12	1-----CONTROL
A			
A	1.28583	12	3--1.0_mg/kg/day
A			
A	1.26800	12	2--0.1_mg/kg/day

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ARGUS DEVELOPMENTAL NEURO PND12 CNS MORPHOMETRICS  
PROC GLM - WITH TUKEYS

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## General Linear Models Procedure

Tukey's Studentized Range (HSD) Test for variable: CEREBRUM

NOTE: This test controls the type I experimentwise error rate, but generally has a higher type II error rate than REGWQ.

Alpha= 0.05 df= 30 MSE= 0.0955  
Critical Value of Studentized Range= 3.487  
Minimum Significant Difference= 0.311

Means with the same letter are not significantly different.

Tukey Grouping	Mean	N	TRT
A	12.8583	12	3--1.0_mg/kg/day
A	12.8417	12	1-----CONTROL
A	12.8083	12	2--0.1_mg/kg/day

1

ARGUS DEVELOPMENTAL NEURO PND12 CNS MORPHOMETRICS  
PROC GLM - WITH TUKEYS

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## General Linear Models Procedure

Tukey's Studentized Range (HSD) Test for variable: APCBLM

NOTE: This test controls the type I experimentwise error rate, but generally has a higher type II error rate than REGWQ.

Alpha= 0.05 df= 30 MSE= 0.098111  
Critical Value of Studentized Range= 3.487  
Minimum Significant Difference= 0.3153

Means with the same letter are not significantly different.

Tukey Grouping	Mean	N	TRT
A	3.5667	12	2--0.1_mg/kg/day
B	3.1500	12	1-----CONTROL
B	3.0500	12	3--1.0_mg/kg/day

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ARGUS DEVELOPMENTAL NEURO PND12 CNS MORPHOMETRICS  
PROC GLM - WITH TUKEYS

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## General Linear Models Procedure

Tukey's Studentized Range (HSD) Test for variable: FCORTEX

NOTE: This test controls the type I experimentwise error rate, but generally has a higher type II error rate than REGWQ.

Alpha= 0.05 df= 30 MSE= 37004.91  
Critical Value of Studentized Range= 3.487  
Minimum Significant Difference= 193.61

Means with the same letter are not significantly different.

Tukey Grouping	Mean	N	TRT
A	1450.00	12	2--0.1_mg/kg/day
A			
A	1430.00	12	1-----CONTROL
A			
A	1425.17	12	3--1.0_mg/kg/day

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ARGUS DEVELOPMENTAL NEURO PND12 CNS MORPHOMETRICS  
PROC GLM - WITH TUKEYS

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## General Linear Models Procedure

Tukey's Studentized Range (HSD) Test for variable: PCORTEX

NOTE: This test controls the type I 'experimentwise error rate, but generally has a higher type II error rate than REGWQ.

Alpha= 0.05 df= 30 MSE= 8051.2  
Critical Value of Studentized Range= 3.487  
Minimum Significant Difference= 90.309

Means with the same letter are not significantly different.

Tukey Grouping	Mean	N	TRT
A	1470.00	12	3--1.0_mg/kg/day
A			
A	1450.00	12	2--0.1_mg/kg/day
A			
A	1428.00	12	1-----CONTROL

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ARGUS DEVELOPMENTAL NEURO PND12 CNS MORPHOMETRICS  
PROC GLM - WITH TUKEYS

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## General Linear Models Procedure

Tukey's Studentized Range (HSD) Test for variable: CAUDPUT

NOTE: This test controls the type I experimentwise error rate, but generally has a higher type II error rate than REGWQ.

Alpha= 0.05 df= 30 MSE= 15449.6  
Critical Value of Studentized Range= 3.487  
Minimum Significant Difference= 125.1

Means with the same letter are not significantly different.

Tukey Grouping	Mean	N	TRT
A	2428.00	12	3--1.0 mg/kg/day
A	2408.00	12	1-----CONTROL
B	2232.00	12	2--0.1 mg/kg/day

1

ARGUS DEVELOPMENTAL NEURO PND12 CNS MORPHOMETRICS  
PROC GLM - WITH TUKEYS

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## General Linear Models Procedure

Tukey's Studentized Range (HSD) Test for variable: CORPCOL

NOTE: This test controls the type I experimentwise error rate, but generally has a higher type II error rate than REGWQ.

Alpha= 0.05 df= 30 MSE= 3655.322  
Critical Value of Studentized Range= 3.487  
Minimum Significant Difference= 60.85

Means with the same letter are not significantly different.

Tukey Grouping	Mean	N	TRT
A	366.42	12	3--1.0_mg/kg/day
B	288.00	12	1-----CONTROL
B	278.42	12	2--0.1_mg/kg/day

1

ARGUS DEVELOPMENTAL NEURO PND12 CNS MORPHOMETRICS  
PROC GLM - WITH TUKEYS

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## General Linear Models Procedure

## Tukey's Studentized Range (HSD) Test for variable: HIPPO

NOTE: This test controls the type I experimentwise error rate, but generally has a higher type II error rate than REGWQ.

Alpha= 0.05 df= 30 MSE= 7180.8  
Critical Value of Studentized Range= 3.487  
Minimum Significant Difference= 85.288

Means with the same letter are not significantly different.

Tukey Grouping	Mean	N	TRT
A	1074.00	12	3--1.0_mg/kg/day
A	1066.00	12	1-----CONTROL
B	936.00	12	2--0.1_mg/kg/day

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ARGUS DEVELOPMENTAL NEURO PND12 CNS MORPHOMETRICS  
PROC GLM - WITH TUKEYS

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## General Linear Models Procedure

Tukey's Studentized Range (HSD) Test for variable: CEREBLL

NOTE: This test controls the type I experimentwise error rate, but generally has a higher type II error rate than REGWQ.

Alpha= 0.05 df= 30 MSE= 65638.4  
Critical Value of Studentized Range= 3.487  
Minimum Significant Difference= 257.86

Means with the same letter are not significantly different.

Tukey Grouping	Mean	N	TRT
A	3556.0	12	1-----CONTROL
A	3396.0	12	3--1.0_mg/kg/day
A	3392.0	12	2--0.1_mg/kg/day

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ARGUS DEVELOPMENTAL NEURO PND12 CNS MORPHOMETRICS  
PROC GLM - WITH TUKEYS

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## General Linear Models Procedure

Tukey's Studentized Range (HSD) Test for variable: XGEM

NOTE: This test controls the type I experimentwise error rate, but generally has a higher type II error rate than REGWQ.

Alpha= 0.05 df= 30 MSE= 15.73333  
Critical Value of Studentized Range= 3.487  
Minimum Significant Difference= 3.9922

Means with the same letter are not significantly different.

Tukey Grouping	Mean	N	TRT
A	40.083	12	1-----CONTROL
A	39.083	12	2--0.1_mg/kg/day
A	38.500	12	3--1.0_mg/kg/day